

*AAU Association of American Universities*  
*COGR Council on Governmental Relations*  
*NASULGC National Association of State Universities and Land-Grant Colleges*

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March 2, 2001

National Human Research Protection Advisory Committee (NHRPAC)  
Attn: Dr. Greg Koski  
6100 Executive Boulevard, Suite 3B01  
MSC-7507  
Rockville MD 20892-7507

Dear Dr. Koski,

The Office of Human Research Protection (OHRP) recently placed a document on its website with a request for comment. The document, labeled "draft interim guidance," is entitled "Financial Relationships in Clinical Research: Issues for Institutions, Clinical Investigators, and IRBs to Consider When Dealing with Issues of Financial Interests and Human Subjects Protection" (referred to hereafter as Guidance). Our three associations, which represent key segments of the academic community concerned with regulatory compliance in this area, provide comment on this unusual interim (effective "when?") draft guidance document because of the seriousness of the issue. We are concerned for substantive as well as procedural reasons.

This letter presents comments of the Association of American Universities (AAU), the Council on Governmental Relations (COGR), and the National Association of State Universities and Land-Grant Colleges (NASULGC). The AAU is an organization of public and private research universities devoted to maintaining a strong system of academic research and education, and consists of 59 U.S. universities and 2 Canadian universities. COGR is an association of 143 research-intensive universities that concerns itself with the influence of government regulations, policies, and practices on the performance of research conducted at colleges and universities. NASULGC, with roots back to 1887, is the nation's oldest nonprofit higher education association with 210 members from all 50 states, the District of Columbia, and the U.S. territories. NASULGC's mission is to support high-quality public education and to enhance the ability of its members to carry out their land-grant heritage in learning, discovery, and engagement with society at large.

General Comment and Request to Withdraw

We stand firmly behind OHRP in support of the vital importance of human subject protection. The protection of human research participants is a fundamental institutional obligation, as shown by the central role the Institutional Review Boards (IRBs) play in our research universities. The protection of human subjects and the obligation to protect the integrity of the research process merit equal attention and have equal standing within the university. They are currently guarded by individual federal regulations, with which universities are bound to comply. The proposed guidance seems to advocate precipitous changes in one area, i.e., human subjects protection, by imposing new requirements regarding safeguarding against individual and institutional financial conflicts. We agree that these financial issues need to be addressed, but in their own broad context, and with due consideration. Given its overly prescriptive tone, this guidance document comes at an unfortunate time, since universities have made a commitment to, and are in the midst of, a general review of their existing systems to protect human participants in research and to guard the objectivity of research.

March 2, 2001

Page Two

The guidance contains a mixture of observations, opinions, commentary and recommendations. This may be due to the fact that the guidance is intended to be a summary of the meeting convened on August 15-16, 2000, by HHS. Our membership recognizes in the guidance a reflection of many relevant opinions expressed at the meeting, but neither is it a summary, nor does it reflect a consensus. In some cases, statements seem to be based on anecdotal evidence, in others proposed new requirements would place universities in conflict with existing regulations. We therefore consider it premature to designate the document as interim guidance, even in draft form.

We believe OHRP should distinguish between those areas which have been considered extensively, such as the management of conflicts of individual investigators, and those areas which are not yet well developed and which represent entirely new policy, such as oversight of institutional conflicts of interest. We believe a better way to inform the debate would be for OHRP to withdraw the current guidance and for HHS to reissue portions of it as points for consideration. Such a document might build on the current momentum of university review of these issues. Such a "points for consideration" document might seek responses to alternatives, which might provide to the government a broader fact basis upon which to gauge what is required to build community consensus prior to advocating policy changes or revised rules. Offering candidate points for consideration, rather than the prescription contained in the current draft interim guidance, would supplement rather than complicate the ongoing presidential-level initiatives underway by the AAU and other leaders in the academic community. Hoping that you will embrace this suggestion, we offer several more detailed observations that address the issues raised in the current draft.

#### Substantive Comments

We recognize that universities are currently subject to two different sets of regulations, issued under the authority of different statutes. One covers the protection of human subjects, the other addresses the prevention, disclosure, and management of financial conflicts of interest in order to protect the objectivity of research. There is currently no overarching regulation that combines both. It could be a point for consideration whether new regulation would be necessary for the existing systems to be synchronized, or whether it is a matter of strengthening linkages among the existing IRB Committees, Officials or Committees Responsible for Conflict of Interest, Technology Transfer Offices and Central Administration Offices, or even building new internal institutional bridges. Many universities have been working to build such internal bridges in recent years, and these efforts have been redoubled since the August meeting raised university consciousness further.

Current HHS conflict of interest regulations are not intended to prohibit the beneficial activities that can give rise to conflicts. Instead, the current regulations recognize that financial conflicts are an inevitable result of many diverse activities within the university and the public. Current HHS regulations are premised on detecting and managing financial conflicts, or, should that prove impossible, rejecting a proposed project altogether; the draft interim guidance appears to be at odds with this premise. It might be a point for consideration whether in clinical trials different measures might be needed in order to assure patients' health

March 2, 2001

Page Three

and protection from those needed in basic research projects. It might also be a point for consideration whether the current regulations on financial conflicts might need to be revised in view of the potential adverse impact of new forms and an increased volume of financial compensation, or even whether a government-wide policy can be promulgated at this time.

Neither the current HHS regulations on human subject protection nor those on conflict of interest put IRBs in control of conflict of interest procedures, yet the draft interim guidance does in some cases. It might be a point for consideration what the reasonable level of tolerance for workload and expertise for an IRB should be, and to what extent existing divisions of expertise between IRBs and conflict-of-interest processes offer the best overall assurance for the university – or whether changes in this regulatory framework are necessary. It already is a serious point of debate among the community to what extent detail about financial disclosures should be a part of the research protocol and informed consent.

Finally, the guidance makes a foray into an area in which regulations are not yet promulgated: institutional conflicts of interest. OHRP, as an advocate of human subjects protection, could add valuable points for consideration. This area is fraught with complexities, and many other considerations will have to be taken into account to capture the institutional obligations. Intense high-level discussions are underway in the university community. The AAU and the AAMC have committed to developing principles to help guide member institutions in this delicate area. In light of this, we believe that the OHRP draft should support the debate rather than attempt to direct it prematurely.

#### Procedural Comments

During the past several months, the university community has experienced increased confusion about HHS' process for promulgating regulations vs. guidance. This is partly due to the precipitous issuance of new proposed regulations and guidance, aggravated by the fact that the Administration transition placed some of these regulations on hold pending review. Confusion, however, also arose because of the issuance of "guidance," which, due to attached sanctions, resembled substantive rules, some of which were later withdrawn. Misunderstanding can also arise when interim guidance is issued in draft. We ask OHRP not to increase the anxiety and uncertainty in this area.

The process for review and comment of Executive Branch rulemaking is clearly established by the Administrative Procedures Act. If binding new requirements are to be considered, they must be based on clear evidence, not anecdotal statements or one-sided views voiced at a conference, and we trust that future endeavors in this field will be expressed in the established format. Substantial new responsibilities, such as those described in the interim draft guidance for IRBs, are too extensive to be announced as guidance, in draft or otherwise. We understand that OHRP has HHS-wide authority for protection of human subjects and a leadership position on this issue government-wide. However, in view of the financial conflicts-of-interest part of the issue, we suggest that subsequent guidance or requests for comment be prepared and issued on behalf of

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March 2, 2001

Page Four

HHS as a whole instead of on behalf of one of its constituent parts, or preferably that a dialogue be initiated to arrive at a government-wide consideration of future new policy or regulations.

Conclusion

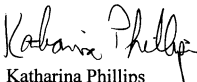
In this important area of protecting human life and managing financial conflicts, it is essential that the community reach consensus with the government and that the government, if possible, speak with one voice. We suggest HHS consider convening a follow-on conference, in the summer or fall of 2001, perhaps in conjunction with other interested federal agencies and others in the academic community. The agenda to such a conference could be prompted by points of consideration from OHRP developed jointly with other affected parties within HHS (e.g., ORI and NIH). On a broader basis, it would invite the academic community to report on changes in policy and procedures, which it has considered or implemented since the beginning of the serious debate one year ago. This conference, with the goal of assessing the degree of consensus on required protections, could be an important milestone in the dialogue among all parties towards further policy development in the area of financial conflicts of interest and human subjects protection.

We appreciate this opportunity to offer our thoughts, and have appreciated the seriousness with which you and your office have been taking the views of the community into account.

Cordially,



Nils Hasselmo  
President, AAU



Katharina Phillips  
President, COGR



C. Peter Magrath  
President, NASULGC

NH/RJT/hc

cc: Ruth Kirschstein, M.D.  
Acting Director, NIH

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